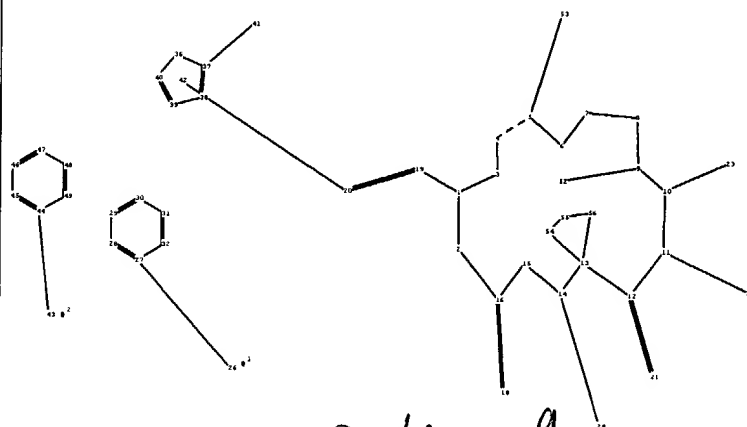
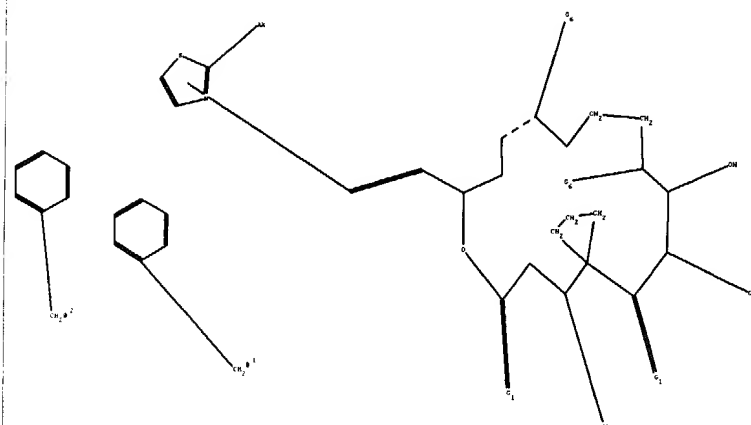


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452603/44523  
↓  
09485292



paper no. 9

chain nodes :

18 19 20 21 23 24 26 35 41 43 52 53

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 27 28 29 30 31  
32 36 37 38 39 40 44 45 46 47 48 49 54 55 56

chain bonds :

1-19 5-53 9-52 10-23 11-35 12-21 14-24 16-18 19-20 26-27 37-41  
43-44

ring bonds :

1-2 1-3 2-16 3-4 4-5 5-6 6-7 7-8 8-9 9-10 10-11 11-12 12-13  
13-14 13-56 13-54 14-15 15-16 27-28 27-32 28-29 29-30 30-31  
31-32 36-37 36-40 37-38 38-39 39-40 44-45 44-49 45-46 46-47  
47-48 48-49 54-55 55-56

exact/norm bonds :

4-5 5-6 5-53 9-52 10-23 11-35 12-21 13-56 13-54 14-24 16-18  
37-38 37-41 38-39 54-55 55-56

exact bonds :

1-2 1-3 1-19 2-16 3-4 6-7 7-8 8-9 9-10 10-11 11-12 12-13  
13-14 14-15 15-16 19-20 26-27 36-37 36-40 39-40 43-44

normalized bonds :

27-28 27-32 28-29 29-30 30-31 31-32 44-45 44-49 45-46 46-47  
47-48 48-49

isolated ring systems :

containing 27 : 36 : 44 :

G1:O,S

G2: Ak, Ph, [\*1]

G6: Ph, Ak, H, [\*2]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom  
10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 18:CLASS  
19:CLASS 20:CLASS 21:CLASS 23:CLASS 24:CLASS 26:CLASS 27:Atom  
28:Atom 29:Atom 30:Atom 31:Atom 32:Atom 35:CLASS 36:Atom 37:Atom  
38:Atom 39:Atom 40:Atom 41:CLASS 42:CLASS 43:CLASS 44:Atom 45:Atom  
46:Atom 47:Atom 48:Atom 49:Atom 52:CLASS 53:CLASS 54:CLASS  
55:CLASS 56:CLASS

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America  
 NEWS 2 "Ask CAS" for self-help around the clock  
 NEWS 3 JAN 27 Source of Registration (SR) information in REGISTRY updated  
 and searchable  
 NEWS 4 JAN 27 A new search aid, the Company Name Thesaurus, available in  
 CA/CAPLUS  
 NEWS 5 FEB 05 German (DE) application and patent publication number format  
 changes  
 NEWS 6 MAR 03 MEDLINE and LMEEDLINE reloaded  
 NEWS 7 MAR 03 MEDLINE file segment of TOXCENTER reloaded  
 NEWS 8 MAR 03 FRANCEPAT now available on STN  
 NEWS 9 MAR 29 Pharmaceutical Substances (PS) now available on STN  
 NEWS 10 MAR 29 WPIFV now available on STN  
 NEWS 11 MAR 29 New monthly current-awareness alert (SDI) frequency in RAPRA  
 NEWS 12 APR 26 PROMT: New display field available  
 NEWS 13 APR 26 IFIPAT/IFIUDB/IFICDB: New super search and display field  
 available  
 NEWS 14 APR 26 LITALERT now available on STN  
 NEWS 15 APR 27 NLDB: New search and display fields available  
 NEWS 16 May 10 PROUSDDR now available on STN  
 NEWS 17 May 19 PROUSDDR: One FREE connect hour, per account, in both May  
 and June 2004  
 NEWS 18 May 12 EXTEND option available in structure searching  
 NEWS 19 May 12 Polymer links for the POLYLINK command completed in REGISTRY  
 NEWS 20 May 17 FRFULL now available on STN

NEWS EXPRESS MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT  
 MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
 AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004

NEWS HOURS STN Operating Hours Plus Help Desk Availability  
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 NEWS PHONE Direct Dial and Telecommunication Network Access to STN  
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FILE 'HOME' ENTERED AT 16:55:55 ON 25 MAY 2004

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 16:56:02 ON 25 MAY 2004

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 24 MAY 2004 HIGHEST RN 685504-43-2  
 DICTIONARY FILE UPDATES: 24 MAY 2004 HIGHEST RN 685504-43-2

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See [HELP CROSSOVER](#) for details.

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<http://www.cas.org/ONLINE/DBSS/registryss.html>

=>

L2 STRUCTURE UPLOADED

=> d 12

L2 HAS NO ANSWERS

L2 STR

=> s 12

SAMPLE SEARCH INITIATED 16:58:19 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 6 TO ITERATE

100.0% PROCESSED 6 ITERATIONS

1 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 6 TO 266

PROJECTED ANSWERS: 1 TO 80

L3 1 SEA SSS SAM L2

=> s 12 full

THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS

DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y

FULL SEARCH INITIATED 16:58:24 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 152 TO ITERATE

100.0% PROCESSED 152 ITERATIONS

57 ANSWERS

SEARCH TIME: 00.00.01

L4 57 SEA SSS FUL L2

=> file hcaplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

156.68

156.89

FILE 'HCAPLUS' ENTERED AT 16:58:27 ON 25 MAY 2004

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FILE COVERS 1907 - 25 May 2004 VOL 140 ISS 22  
FILE LAST UPDATED: 24 May 2004 (20040524/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 14

L5 8 L4

=> s 15 and klar, u?/au

70 KLAR, U?/AU

L6 7 L5 AND KLAR, U?/AU

=> d 16, ibib abs fhitr, 1-7

L6 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
-----------	-------------------

ACCESSION NUMBER:	2003:693140 HCAPLUS
DOCUMENT NUMBER:	139:191465
TITLE:	Use of epothilones in the treatment of brain diseases associated with proliferative processes
INVENTOR(S):	Lichtner, Rosemarie; Rotgeri, Andrea; Buchmann, Bernd; Hoffmann, Karin; <b>Klar, Ulrich</b> ; Schwede, Wolfgang; Skuballa, Werner
PATENT ASSIGNEE(S):	Schering Aktiengesellschaft, Germany
SOURCE:	Eur. Pat. Appl., 27 pp. CODEN: EPXXDW
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2
<u>PATENT INFORMATION:</u>	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1340498	A1	20030903	EP 2002-4745	20020301
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
WO 2003074053	A1	20030912	WO 2003-EP2085	20030228
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,				

NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,  
ML, MR, NE, SN, TD, TG

US 2004019088 A1 20040129 US 2003-375043 20030228  
PRIORITY APPLN. INFO.: EP 2002-4745 A 20020301  
US 2002-361062P P 20020301

OTHER SOURCE(S): MARPAT 139:191465

AB The invention provides the use of an epothilone, which shows an av. distribution coeff. between plasma and brain of 0.3-1.5 in the mouse i.v. bolus injection assay, for the prepn. of a medicament for the treatment of a brain disease assocd. with proliferative processes.

IT **289502-84-7**

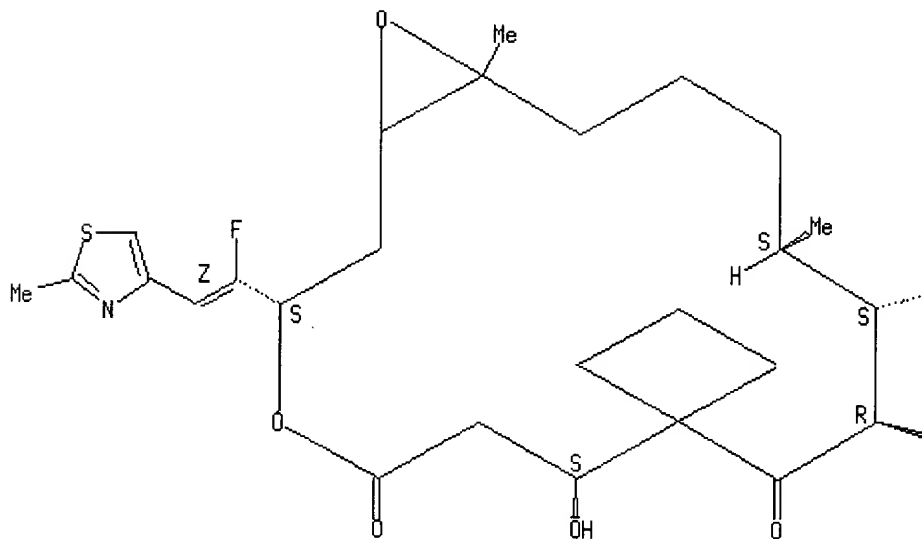
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(epothilones for treatment of brain diseases assocd. with proliferative processes)

RN **289502-84-7** HCAPLUS

CN Spiro[cyclobutane-1,8'-[4,17]dioxabicyclo[14.1.0]heptadecane]-5',9'-dione, 3'-[(1Z)-1-fluoro-2-(2-methyl-4-thiazolyl)ethenyl]-7',11'-dihydroxy-10',12',16'-trimethyl-, (3'S,7'S,10'R,11'S,12'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

OH

Me

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 2000:790507 HCAPLUS  
DOCUMENT NUMBER: 133:362656  
TITLE: Preparation of 6-alkenyl-, 6-alkynyl- and 6-epoxyepothilone derivatives and their antitumor activity  
INVENTOR(S): **Klar, Ulrich**; Schwede, Wolfgang; Skuballa, Werner; Buchmann, Bernd; Hoffmann, Jens; Lichtner, Rosemarie  
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany  
SOURCE: PCT Int. Appl., 298 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066589	A1	20001109	WO 2000-IB657	20000501
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
DE 19921086	A1	20001102	DE 1999-19921086	19990430
DE 19954228	A1	20010913	DE 1999-19954228	19991104
DE 10015836	A1	20011011	DE 2000-10015836	20000327
BR 2000010190	A	20020108	BR 2000-10190	20000501
EP 1173441	A1	20020123	EP 2000-922826	20000501
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO			
JP 2002543203	T2	20021217	JP 2000-615619	20000501
EE 200100568	A	20030217	EE 2001-568	20000501
NZ 514989	A	20040227	NZ 2000-514989	20000501

BG 106053	A	20020531	BG 2001-106053	20011026
NO 2001005278	A	20011221	NO 2001-5278	20011029
PRIORITY APPLN. INFO.:			DE 1999-19921086	A1 19990430
			DE 1999-19954228	A1 19991104
			DE 2000-10015836	A1 20000327
			WO 2000-IB657	W 20000501

OTHER SOURCE(S):           MARPAT 133:362656

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The antitumor agents, 6-alkenyl-, 6-alkynyl- and 6-epoxyepothilones I (R1a, R1b are same or different = H, C1-C10 alkyl, C6-C12 aryl, C7-C20 aralkyl each optionally substituted; or together = (CH2)<sub>m</sub> m = 1-5 or -CH2OCH2-; R2a(R2b replace a with b) = H, substituted alkyl, aryl, aralkyl, (CH2)<sub>ra</sub>-C≡(or =)C-(CH2)<sub>pa</sub>-R26a, Q, Q1 where n = 0-5; ra, rb = the same or different and = 0-4; pa, pb = the same or different and = 0-3; R3a = H, substituted alkyl, aryl or aralkyl; R3b = OH, OPG14; R14 = H, OR14a, halogen and R14a = H, SO2-alkyl, SO2-aryl or SO2-aralkyl; R4 = H, substituted alkyl, aryl or aralkyl, halogen, OR25, CN; R26a, R26b = same or different = H, substituted alkyl, aryl or aralkyl, C1-C10 acyl or if pa or pb > 0, addnl. a group OR27; R25 = R27 = R22 = H, PG; R5 = H, substituted alkyl, aryl or aralkyl, (CH2)<sub>s</sub>T s = 1-4, T = OR22 or halogen; R6, R7 = H or together = bond or O; G = X=CR8 or bi- or tricyclic aryl radical and R8 = H, halogen, CN, or substituted alkyl, aryl or aralkyl; X = O, two OR23 groups, C2-C10-alkylene- $\alpha,\omega$ -dioxy straight chain or branched; H/OR9 or CR10R11 group and R23 = alkyl radical, R9 = H, PG, R10,R11 = same or different = H, substituted alkyl, aryl or aralkyl, or together with the methylene are a 5-7 carbocyclic ring; D-E = CH2CH2 or OCH2; A = OC(O), OCH2, CH2C(O), NR29C(O), NR29SO2 and R29 = H, alkyl; Z = O or H/OR12 and R12 = H, PG) were prepd. Thus II was prepd. in a multistep synthesis starting from (4S)-4-(2-methyl-1-oxoprop-2-yl)-2,2-dimethyl[1,3]dioxane and 5-trimethylsilylpent-4-in-1-yl magnesium bromide. II had an IC50 value [nM] of 3.0 for the growth inhibition of human MCF-7 breast- and 75 for multidrug resistant NCI/ADR carcinoma cell lines with a selectivity of 2.5. The new epothilone derivs. interact with tubulin by stabilizing microtubuli that are formed. They are able to influence the cell-splitting in a phase-specific manner and are therefore useful in treating diseases or conditions assocd. with the need for cell growth, division and/or proliferation. Thus the epothilone derivs. are suitable for treating malignant tumors, e.g., ovarian, stomach, colon, adeno-, breast, lung, head and neck carcinomas, malignant melanoma, acute lymphocytic and myelocytic leukemia; and for anti-angiogenesis therapy as well as for treatment of chronic inflammatory diseases (such as psoriasis, arthritis).

IT 305842-49-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of 6-alkenyl-, 6-alkynyl- and 6-epoxyepothilone derivs. and their use in pharmaceutical preps.)

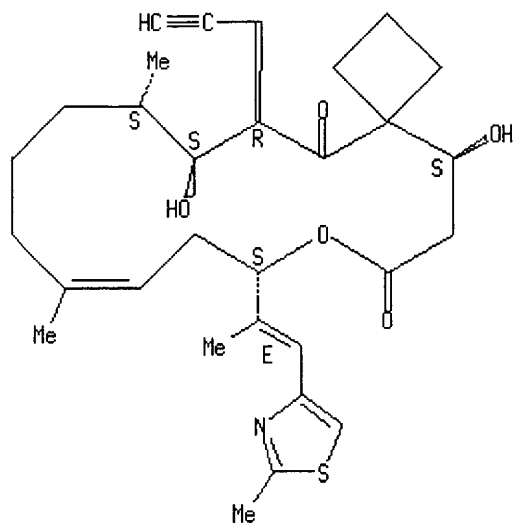
RN 305842-49-3 HCAPLUS

CN 8-Oxaspiro[3.15]nonadec-11-ene-7,19-dione, 5,17-dihydroxy-12,16-dimethyl-9-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-18-(2-propynyl)-, (5S,9S,16S,17S,18R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Double bond geometry as described by E or Z.



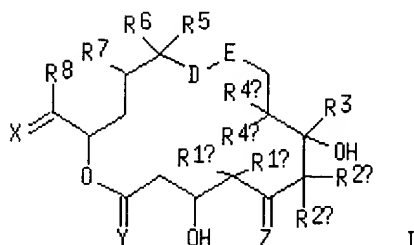
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

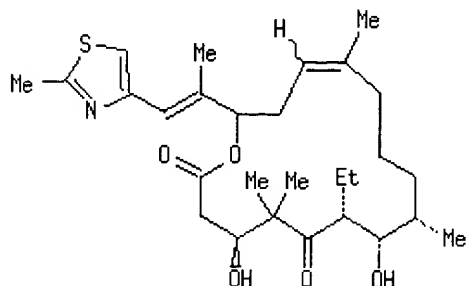
Full Text Citing References

ACCESSION NUMBER: 2000:738730 HCAPLUS  
 DOCUMENT NUMBER: 133:309795  
 TITLE: Preparation of new epothilone derivatives and their pharmaceutical uses  
 INVENTOR(S): Klar, Ulrich; Schwede, Wolfgang; Skuballa, Werner; Buchmann, Bernd; Schirner, Michael  
 PATENT ASSIGNEE(S): Schering A.-G., Germany  
 SOURCE: Ger. Offen., 74 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19908767	A1	20001019	DE 1999-19908767	19990218
PRIORITY APPLN. INFO.:			DE 1999-19908767	19990218
OTHER SOURCE(S):			MARPAT 133:309795	
GI				



I



II

AB New epothilone derivs. I (R1a,R1b = R2a,R2b = same or different H, alkyl, aryl, aralkyl or (CH<sub>2</sub>)<sub>m,n</sub>, m, n = 2-5; R3 = H, alkyl, aryl, aralkyl; R4a,R4b = same or different H, alkyl, aryl, aralkyl or (CH<sub>2</sub>)<sub>p</sub> = 2-5, CH<sub>2</sub>CH<sub>2</sub>, CH=CH, C≡C, epoxy, CH(OH)CH(OH), CH(OH)CH<sub>2</sub>; D-E = a group; R5 = H, alkyl, aryl, aralkyl; R6,R7 = H, bond, O; R8 = H, alkyl, aryl, aralkyl; X = O, OR<sub>23</sub> alkylene- $\alpha$ , $\omega$ -dioxy group straight or branched, OR<sub>9</sub> or the CR<sub>10</sub>R<sub>11</sub> group where R<sub>23</sub> = alkyl, R<sub>9</sub> = H or protecting group and R<sub>10</sub>,R<sub>11</sub> = same or different H, alkyl, aryl, aralkyl or R<sub>10</sub>,R<sub>11</sub> = together with methylene are a 5-7 membered carbocyclic ring; Y = O or two H; Z = O or H/OR<sub>12</sub> and R<sub>12</sub> = H or a protecting group) were prepd. Thus E- and Z-II were prepd. via a multistep synthesis. I cooperate with tubulin by stabilizing formed microtubuli. I are able phase specifically to affect the cell division and are suitable for the treatment of malignant ovarian, stomach, colon, adeno, breast, lung, head and neck tumors, malignant melanomas, acute lymphocytic and myelocytic leukemia. Derivs. of I are suitable for use in anti-angiogenic therapy as well as for treating chronic inflammatory diseases (psoriasis, arthritis). In order to prevent uncontrolled cell proliferations and to improve the compatibility of medical implants I can be applied or incorporated into polymeric materials. I can be used alone or to achieve additive or synergistic effects in combination with further principles and substance classes applicable in tumor therapy.

IT 220773-96-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

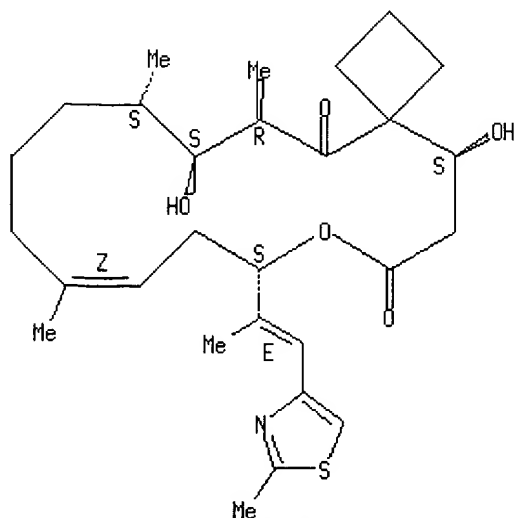
(prepn. of new epothilone derivs. and their pharmaceutical uses)

RN 220773-96-6 HCAPLUS

CN 8-Oxaspiro[3.15]nonadec-11-ene-7,19-dione, 5,17-dihydroxy-12,16,18-trimethyl-9-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (5S,9S,11Z,16S,17S,18R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L6 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

Full  
Text

Citing  
References

ACCESSION NUMBER: 2000:592721 HCAPLUS  
DOCUMENT NUMBER: 133:193028  
TITLE: Preparation of 16-halogen epothilone derivatives and their use as antitumor agents  
INVENTOR(S): Klar, Ulrich; Skuballa, Werner; Buchmann, Bernd; Schwede, Wolfgang; Schirner, Michael  
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany  
SOURCE: PCT Int. Appl., 105 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

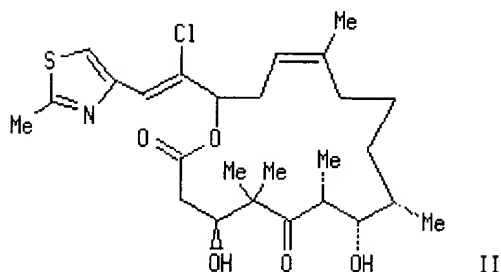
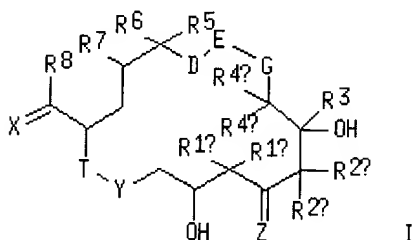
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000049021	A2	20000824	WO 2000-EP1333	20000218
WO 2000049021	A3	20001228		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19908765	A1	20000824	DE 1999-19908765	19990218
DE 19954230	A1	20011115	DE 1999-19954230	19991104
EP 1150980	A2	20011107	EP 2000-909205	20000218
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BR 2000008331	A	20020129	BR 2000-8331	20000218
JP 2002537301	T2	20021105	JP 2000-599760	20000218
EE 200100431	A	20021216	EE 2001-431	20000218
BG 105802	A	20020329	BG 2001-105802	20010809
NO 2001004013	A	20011018	NO 2001-4013	20010817
ZA 2001007648	A	20030107	ZA 2001-7648	20010917

US 6610736  
US 2004014978  
PRIORITY APPLN. INFO.:

B1 20030826  
A1 20040122

US 2001-913495 20011207  
US 2003-364337 20030212  
DE 1999-19908765 A 19990218  
DE 1999-19954230 A 19991104  
WO 2000-EP1333 W 20000218  
US 2001-913495 A3 20011207

OTHER SOURCE(S): MARPAT 133:193028  
GI



AB 16-Halogen epothilone derivs. I (R1a, R1b = R2a, R2b = H, C1-C10-alkyl, aryl, C7-C20-aralkyl, (CH2)<sub>m</sub> m = 2-5; R3 = H, C1-C10-alkyl, aryl, C7-C20-aralkyl; G = O, CH2; R4a, R4b = H, C1-C10-alkyl, aryl, C7-C20-aralkyl, (CH2)<sub>p</sub> p = 2-5; D-E = 1,2-ethanediyl, 1,2-ethenediyl, ethynyl, oxiranyl, 1,2-dihydroxy-1,2-ethanediyl, 1(2)-hydroxy-1,2-ethanediyl, CH2OH; R5 = H, C1-C10-alkyl, aryl, C7-C20-aralkyl, CO2H, CO2-alkyl, CH2OH, CH2O-alkyl, CH2O-acyl, CN, CH2NH2, CH2N(alkyl, acyl)<sub>1,2</sub>, CH2-halogen; R6, R7 = H, bond, O; R8 = halogen, CN; X = O, two alkoxy groups OR23, C2-C10-alkylene- $\alpha,\omega$ -dihydroxy group straight or branched chain, H/OR9, CH10R11 where R23 = C1-C20-alkyl; R9 = H, or protecting group; R10, R11 = H, C1-C10-alkyl, aryl, C7-C20-aralkyl, 5-7 membered carbocyclic ring; T-Y = OC(=O), OCH2, CH2C(=O), NR24C(=O), NR24SO2; R24 = H, C1-C10-alkyl; Z = O, H/OR12 where R12 = H or protecting group) were prep'd. in addn. to all possible stereoisomers and mixts. Thus II was prep'd. from 2-methyl-4-thiazolecarboxaldehyde in a multistep synthesis. The IC<sub>50</sub> of II was 5.1 nM on MCF-7 breast tumor and had an IC<sub>50</sub> of 37 nM on the multidrug resistant carcinoma NCI/ADR.

IT 289501-46-8P

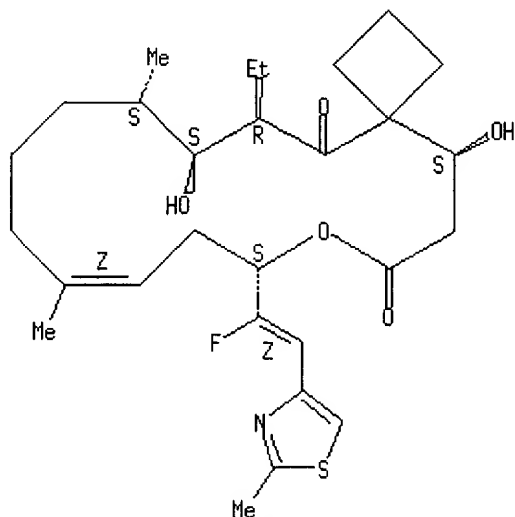
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of 16-halogen epothilone derivs. for use as antitumor agents)

RN 289501-46-8 HCAPLUS

CN 8-Oxaspiro[3.15]nonadec-11-ene-7,19-dione, 18-ethyl-9-[(1Z)-1-fluoro-2-(2-methyl-4-thiazolyl)ethenyl]-5,17-dihydroxy-12,16-dimethyl-, (5S,9S,11Z,16S,17S,18R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L6 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing  
References

ACCESSION NUMBER: 2000:573798 HCAPLUS  
DOCUMENT NUMBER: 133:177064  
TITLE: Preparation of epothilone derivatives useful as pharmaceuticals  
INVENTOR(S): Klar, Ulrich; Skuballa, Werner; Buchmann, Bernd; Schwede, Wolfgang; Schirner, Michael  
PATENT ASSIGNEE(S): Schering A.-G., Germany  
SOURCE: PCT Int. Appl., 141 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

*may need transfer*

*Same as app*

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000047584	A2	20000817	WO 2000-EP1104	20000211
WO 2000047584	A3	20001228		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19907480	A1	20000817	DE 1999-19907480	19990211
CA 2360952	AA	20000817	CA 2000-2360952	20000211
EP 1161430	A2	20011212	EP 2000-920433	20000211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008206	A	20020219	BR 2000-8206	20000211
JP 2002536450	T2	20021029	JP 2000-598504	20000211
EE 200100422	A	20021216	EE 2001-422	20000211

BG 105803	A	20020329	BG 2001-105803	20010809
NO 2001003900	A	20011011	NO 2001-3900	20010810
ZA 2001007458	A	20021210	ZA 2001-7458	20010910
PRIORITY APPLN. INFO.:			DE 1999-19907480	A 19990211
			DE 1999-19954229	A 19991104
			WO 2000-EP1104	W 20000211
OTHER SOURCE(S):		MARPAT 133:177064		
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Novel epothilone derivs. I (R4 = R5 = H, C1-C10 alkyl, aryl, C7-C20 aralkyl; R6, R7 are each H, or together an addnl. bond or O; R8 = Me or H; R1a, R1b together = trimethylene; R2 = Ph, CH2Ph; X = 2-pyridyl, 2-methyl-4-thiazolyl, 2-methyl-4-oxazolyl; or R1a, R1b together = trimethylene; R2 = Me, Et, Pr; X = 2-pyridyl, 2-methyl-4-thiazolyl, 2-methyl-4-oxazolyl; or simultaneously R1a = R1b = Me; R2 = Me, Et, Pr; X = 2-pyridyl, 2-methyl-4-thiazolyl or 2-methyl-4-oxazolyl; and the N and/or S atoms in X can be in an oxidized form; and if R2 and R8 = Me, X can only be a 2-pyridyl residue which is optionally oxidized at the nitrogen atom) and all possible stereoisomers and their mixts were prepd. Thus II was prepd. in a multistep sequence from the starting materials III and IV. The novel compds. interact with tubulin by stabilizing the formed microtubuli. The compds. are able to influence the cell division in a phase-specific manner and are suited for treating malignant tumors, for example, ovarian cancer, gastric carcinoma, colon cancer, breast cancer, lung cancer, head and neck cancer, malignant melanoma, and acute lymphocytic and myelocytic leukemia. The inventive compds. are suited for use in anti-angiogenic therapy as well as for treating chronic inflammatory diseases (psoriasis, arthritis). In order to prevent uncontrolled cell proliferations and to improve the compatibility of medical implants, the inventive compds. can be applied or incorporated in polymeric materials. The inventive compds. can be used alone or, in order to achieve additive or synergistic effects, in conjunction with addnl. constituents and substance classes which can be use in tumor therapy.

IT **288387-10-0P**

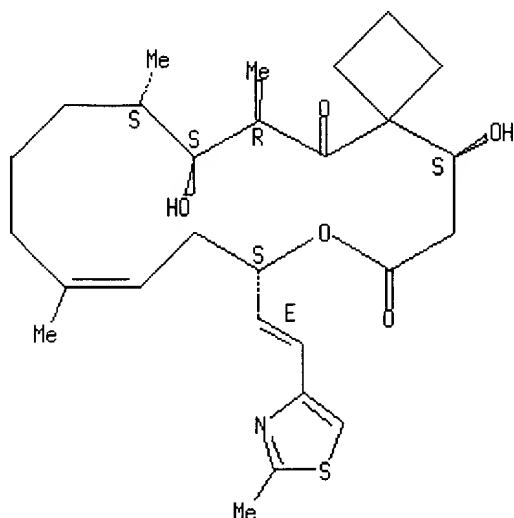
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of epothilone derivs. useful as pharmaceuticals)

RN 288387-10-0 HCAPLUS

CN 8-Oxaspiro[3.15]nonadec-11-ene-7,19-dione, 5,17-dihydroxy-12,16,18-trimethyl-9-[(1E)-2-(2-methyl-4-thiazolyl)ethenyl]-, (5S,9S,16S,17S,18R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as described by E or Z.



L6 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
-----------	-------------------

ACCESSION NUMBER: 2000:15195 HCAPLUS  
 DOCUMENT NUMBER: 132:64110  
 TITLE: The preparation process, intermediate products and pharmaceutical use of epothilone derivatives  
 INVENTOR(S): Buchmann, Bernd; Klar, Ulrich; Skuballa, Werner; Schwede, Wolfgang; Schirner, Michael; Menrad, Andreas  
 PATENT ASSIGNEE(S): Schering A.-G., Germany  
 SOURCE: PCT Int. Appl., 86 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

NO

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000485	A1	20000106	WO 1999-EP4915	19990630
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19830060	A1	20000210	DE 1998-19830060	19980630
DE 19923001	A1	20001116	DE 1999-19923001	19990513
AU 9950369	A1	20000117	AU 1999-50369	19990630
PRIORITY APPLN. INFO.:			DE 1998-19830060	A 19980630
			DE 1999-19923001	A 19990513
			WO 1999-EP4915	W 19990630
OTHER SOURCE(S):			CASREACT 132:64110; MARPAT 132:64110	
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The invention relates to new epothilone derivs. I [R1a, R1b = H, C1-10-alkyl, aryl, C7-10-aralkyl; R1aR1b = (CH<sub>2</sub>)<sub>m</sub>, m = 2 - 5; R2a, R2b = H, C1-10-alkyl, aryl, C7-10-aralkyl; R2aR2b = (CH<sub>2</sub>)<sub>n</sub>, n = 2 - 5; R3 = H, C1-10-alkyl, aryl, C7-10-aralkyl; R4a, R4b = H, C1-10-alkyl, aryl, C7-10-aralkyl; R4aR4b = (CH<sub>2</sub>)<sub>m</sub>, m = 2 - 5; D-E = CH<sub>2</sub>CH<sub>2</sub>, CH:CH, C≡C, oxirane ring, CH(OH)CH(OH), CH(OH)CH<sub>2</sub>; R5 = C1-10-alkyl, aryl, C7-10-aralkyl; R6, R7 = H; R6R7 = O, bond; R8 = C1-10-alkyl, aryl, C7-10-aralkyl; R25 = H, C1-10-alkyl, C1-10-hydroxyalkyl, C1-10-haloalkyl; X = O, (OR<sub>9</sub>)<sub>2</sub>, C2-10-alkylene- $\alpha,\omega$ -dioxo, CR<sub>11</sub>R<sub>12</sub>; CX = CH(OR<sub>10</sub>); R9 = C1-20-alkyl; R10 = H, protecting group; R11, R12 = H, C1-10-alkyl, aryl, C7-10-aralkyl; R11R12 = CH<sub>2</sub>, C5-7-carbocyclic ring; Y = O, CY = CH<sub>2</sub>; CZ = CH(OR<sub>13</sub>), R13 = H, protecting group] which are prepd. via cyclization of ketones II [R15 = H, OH halogen, OR15a, OSO<sub>2</sub>R15b; R15a = H, SO<sub>2</sub>-alkyl, SO<sub>2</sub>-aryl, SO<sub>2</sub>-aralkyl, (CH<sub>2</sub>)<sub>o</sub>, CR16aR16b; R15b = H, C1-20-alkyl, aryl, C7-20-aralkyl; R16a, R16b = H, C1-10-alkyl, aryl, C7-20-aralkyl; R16aR16b = (CH<sub>2</sub>)<sub>q</sub>; o = 2 - 4; q = 3 - 6]. Thus, epothilone deriv. III was prepd. via macrolactonization of carboxylic acid IV with 2,4,6-trichlorobenzoyl chloride and Et<sub>3</sub>N in THF followed by deprotection with aq. CF<sub>3</sub>CO<sub>2</sub>H in CH<sub>2</sub>Cl<sub>2</sub>. I cooperate with tubulin by stabilizing formed microtubuli.

IT **253447-53-9P**

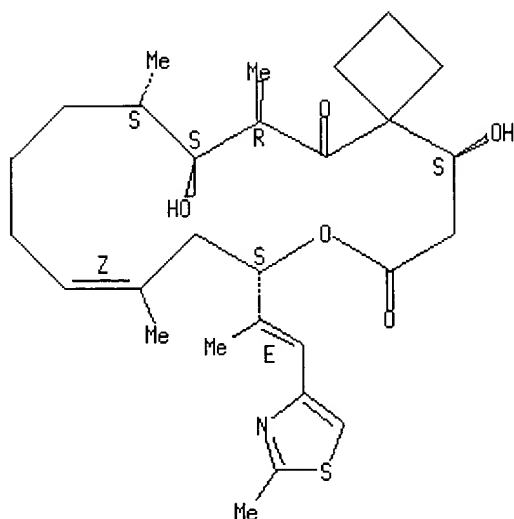
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. and pharmaceutical use of epothilone derivs.)

RN **253447-53-9** HCAPLUS

CN 8-Oxaspiro[3.15]nonadec-11-ene-7,19-dione, 5,17-dihydroxy-11,16,18-trimethyl-9-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (5S,9S,11Z,16S,17S,18R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

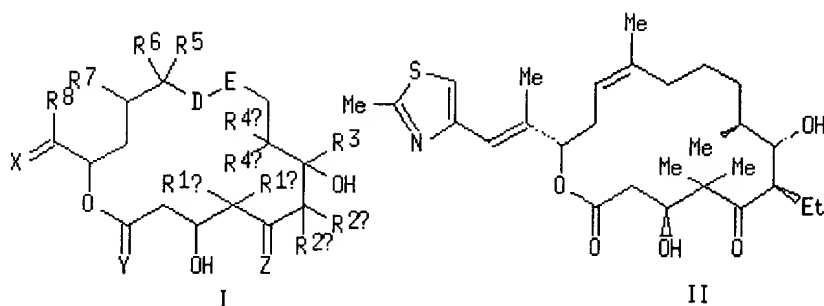
Full Text	Citing References
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ACCESSION NUMBER:	1999:126888	HCAPLUS
DOCUMENT NUMBER:	130:196529	



TITLE: Preparation of new epothilone derivatives as  
pharmaceutical agents  
INVENTOR(S): **Klar, Ulrich**; Schwede, Wolfgang; Skuballa, Werner;  
Buchmann, Bernd; Schirner, Michael  
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany  
SOURCE: PCT Int. Appl., 185 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 4  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 9907692</u>	A2	19990218	<u>WO 1998-EP5064</u>	19980810
<u>WO 9907692</u>	A3	19990514		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
<u>DE 19735574</u>	A1	19990211	<u>DE 1997-19735574</u>	19970809
<u>DE 19735575</u>	A1	19990211	<u>DE 1997-19735575</u>	19970809
<u>DE 19735578</u>	A1	19990211	<u>DE 1997-19735578</u>	19970809
<u>DE 19748928</u>	A1	19990429	<u>DE 1997-19748928</u>	19971024
<u>DE 19749717</u>	A1	19990506	<u>DE 1997-19749717</u>	19971031
<u>DE 19751200</u>	A1	19990520	<u>DE 1997-19751200</u>	19971113
<u>DE 19813821</u>	A1	19990923	<u>DE 1998-19813821</u>	19980320
<u>AU 9893409</u>	A1	19990301	<u>AU 1998-93409</u>	19980810
<u>EP 1005465</u>	A2	20000607	<u>EP 1998-946309</u>	19980810
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
<u>JP 2001512723</u>	T2	20010828	<u>JP 2000-506196</u>	19980810
<u>ZA 9810403</u>	A	20000515	<u>ZA 1998-10403</u>	19981113
<u>US 2003144523</u>	A1	20030731	<u>US 2000-485292</u>	20000503
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			<u>DE 1997-19735575</u>	A 19970809
			<u>DE 1997-19735578</u>	A 19970809
			<u>DE 1997-19748928</u>	A 19971024
			<u>DE 1997-19749717</u>	A 19971031
			<u>DE 1997-19751200</u>	A 19971113
			<u>DE 1998-19813821</u>	A 19980320
			<u>WO 1998-EP5064</u>	W 19980810
OTHER SOURCE(S): MARPAT 130:196529				
GI				



AB Epothilone derivs. of formula I [X = O, alkylene- $\alpha,\omega$ -dioxy, two alkoxy groups, etc.; Y = O, H<sub>2</sub>; Z = O, (H, OH), (H, protected OH); R1a, R1b = H, alkyl, aryl, aralkyl, or together = (CH<sub>2</sub>)<sub>m</sub> where m = 2, 3, 4, 5; R2a, R2b = H, alkyl, aryl, aralkyl, or together = (CH<sub>2</sub>)<sub>n</sub> where n = 2, 3, 4, 5; when D-E = CH<sub>2</sub>CH<sub>2</sub> or when Y = O, R2a or R2b may not be H/Me; R3 = H, alkyl, aryl, aralkyl; R4a, R4b = H, alkyl, aryl, aralkyl, or together = (CH<sub>2</sub>)<sub>p</sub> where p = 2, 3, 4, 5; D-E = CH<sub>2</sub>CH<sub>2</sub>, CH:CH, C $\equiv$ C, 2,3-oxiranediy, CH(OH)CH(OH), CH(OH)CH<sub>2</sub>; R5 = H, alkyl, aryl, aralkyl; R6, R7 = H, together = a satd. bond or O; R8 = H, alkyl, aryl, aralkyl all of which may be substituted] are prepd. Thus, the title compds. (4S,7R,8S,9S,13E,16S(E))- and (4S,7R,8S,9S,13Z,16S(E))-4,8-dihydroxy-7-ethyl-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-1-oxa-5,5,9,13-tetramethylcyclohexadec-13-en-2,6-dione (II) were prepd. in many steps. The new compds. interact with tubulin by stabilizing formed microtubuli. They are capable of influencing cell division in a phase-specific manner and are suitable for the treatment of malignant tumors, such as ovarian, gastric, colon, breast, lung, head and neck carcinoma, adenocarcinoma, malignant melanoma, and acute lymphocytic and myelocytic leukemia. They are also suited for anti-angiogenesis therapy and for the treatment of chronic inflammatory diseases (psoriasis, arthritis). To prevent uncontrolled cell growth on, and for better tolerability of, medical implants, the derivs. can be introduced into or applied to polymeric materials. The compds. provided for in the invention can be used alone or, to achieve additive or synergistic effects, in combination with other principles and substance categories used in tumor therapy.

IT **220773-96-6P**

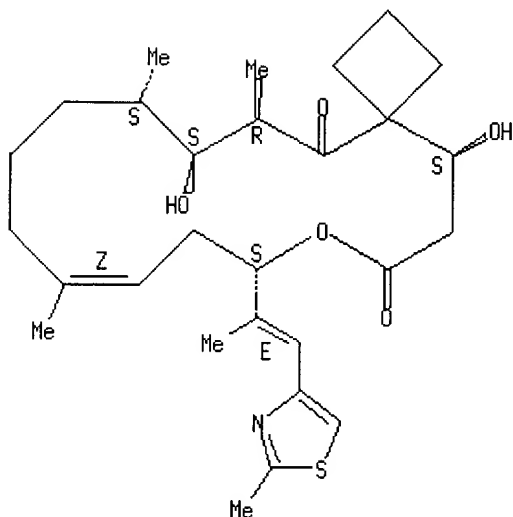
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of epothilone derivs. as antitumor agents)

RN **220773-96-6 HCAPLUS**

CN 8-Oxaspiro[3.15]nonadec-11-ene-7,19-dione, 5,17-dihydroxy-12,16,18-trimethyl-9-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (5S,9S,11Z,16S,17S,18R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



=> file caold

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
35.66	192.55

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
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FILE COVERS 1907-1966

FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

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FILE 'REGISTRY' ENTERED AT 16:56:02 ON 25 MAY 2004

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L4 57 S L2 FULL

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L5 8 S L4

L6 7 S L5 AND KLAR, U?/AU

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=> s 14

L7 0 L4

=> file hcaplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.42	192.97
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-4.85

FILE 'HCAPLUS' ENTERED AT 16:59:19 ON 25 MAY 2004

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FILE COVERS 1907 - 25 May 2004 VOL 140 ISS 22

FILE LAST UPDATED: 24 May 2004 (20040524/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L8 1 L5 NOT L6

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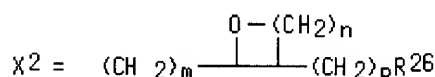
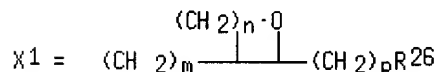
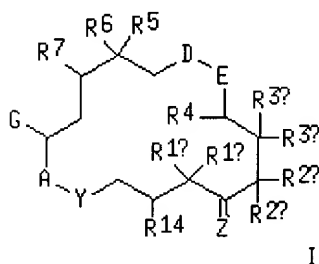
L8 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Citing  
Text References

ACCESSION NUMBER: 2002:157050 HCAPLUS  
DOCUMENT NUMBER: 136:216592  
TITLE: Procedures for the production of 12,13-cyclopropylepothilone derivatives, as well as for their use in pharmaceutical preparations  
PATENT ASSIGNEE(S): Schering Ag, Germany  
SOURCE: Ger. Offen., 64 pp.  
CODEN: GWXXBX  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10041470	A1	20020228	DE 2000-10041470	20000818
PRIORITY APPLN. INFO.:			DE 2000-10041470	20000818
OTHER SOURCE(S):		CASREACT 136:216592; MARPAT 136:216592		

GI



AB The present invention describes new 6-alkenyl- and 6-alkynylepothilone derivs., e.g., I [R1a, R1b = H, C1-10-alkyl, aryl, C7-20-aralkyl; R1aR1b = (CH2)<sub>r</sub>, CH2OCH2; r = 1 - 5; R2a = H, C1-10-alkyl, aryl, C7-20-aralkyl, (CH2)<sub>m</sub>-C≡C-(CH2)<sub>p</sub>R26, (CH2)<sub>m</sub>-C:C-(CH2)<sub>p</sub>R26, X1, X2; n = 0 - 5; p = 0 - 3; m = 0 - 4; R2b = (CH2)<sub>m</sub>-C≡C-(CH2)<sub>p</sub>R26, (CH2)<sub>m</sub>-C:C-(CH2)<sub>p</sub>R26, X1, X2; R3a = H, C1-10-alkyl, aryl, C7-20-aralkyl; R3b = O-protecting group; R4 = H, C1-10-alkyl, aryl, C7-20-aralkyl, halogen, OH, O-protecting group, CN; R5 = H, C1-10-alkyl, aryl, C7-20-aralkyl, (CH2)<sub>s</sub>-T; S = 1 - 4; T = OH, O-protecting group, halogen; R6R7 = C(R33)<sub>2</sub>, NR32 AY = OC(:O), OCH2, CH2C(:O), NR29C(:O), NR29SO2; DE = CH2CH2, CH2O, OCH2; G = X:CR8-, bicyclic or tricyclic aryl; X = O, (O-alkyl)<sub>2</sub>, etc.; Z = H, H,OH, H,O-protective group; R8 = H, halogen, CN, C1-20-alkyl, aryl, C7-20-aralkyl; R14 = H, OH, halogen, O-SO2-alkyl, O-SO2-aryl, O-SO2-aralkyl; R26 = H, C1-10-alkyl, aryl, C7-20-aralkyl, C1-10-acyl, OH, O-protecting group; R29 = H, C1-20-alkyl; R32 = H, C1-4-alkyl, C1-4-acyl; R33 = H, halogen], which interact with tubulins by stabilizing the formed microtubulins (no data). I are able specifically to affect cell division and are suitable, for example for the treatment of malignant tumors ovarian -, stomach -, colon -, adeno -, chest -, lungs -, head and neck carcinoma, malignant melanoma, acute lymphocytic and myelocytic leukemia. In addn. I are suitable for the anti-angiogenesis therapy as well as for the treatment of chronic ignitable illnesses (psoriasis, arthritis). For the avoidance of uncontrolled cell rampant growths on as well as the better compatibility of medical implants I can be up and/or brought into polymers materials. According to invention, I can be used alone or for the achievement of additive or synergistic effects in combination with further principles and substance classes applicable in the tumor therapy. Exptl. data from patents PCT/EP00/01333 and PCT/IB00/00657 are reproduced here.

IT 289501-30-0P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

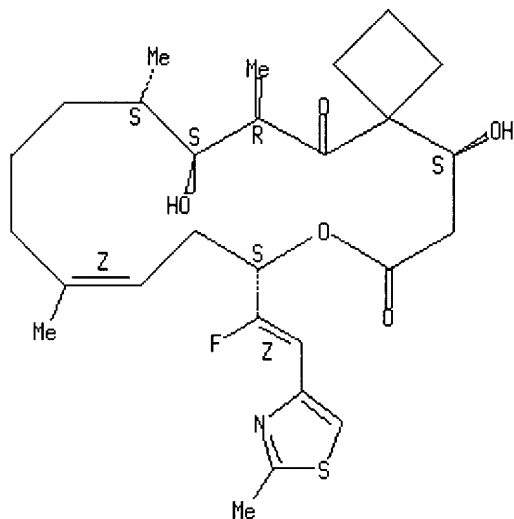
(prepn. of 12,13-cyclopropylepothilone derivs. and their use in pharmaceutical compns.)

RN 289501-30-0 HCAPLUS

CN 8-Oxaspiro[3.15]nonadec-11-ene-7,19-dione, 9-[(1Z)-1-fluoro-2-(2-methyl-4-thiazolyl)ethenyl]-5,17-dihydroxy-12,16,18-trimethyl-, (5S,9S,11Z,16S,17S,18R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



=> file reg

COST IN U.S. DOLLARS

SINCE FILE ENTRY	TOTAL SESSION
------------------	---------------

FULL ESTIMATED COST

7.12	200.09
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE ENTRY	TOTAL SESSION
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CA SUBSCRIBER PRICE

-0.69	-5.54
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FILE 'REGISTRY' ENTERED AT 16:59:35 ON 25 MAY 2004

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 24 MAY 2004 HIGHEST RN 685504-43-2

DICTIONARY FILE UPDATES: 24 MAY 2004 HIGHEST RN 685504-43-2

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See [HELP CROSSOVER](#) for details.

Experimental and calculated property data are now available. For more

information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=>

L9 STRUCTURE UPLOADED

=> d 19

L9 HAS NO ANSWERS

L9 STR

=> s 19

SAMPLE SEARCH INITIATED 17:03:28 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED 1 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 1 TO 80

PROJECTED ANSWERS: 0 TO 0

L10 0 SEA SSS SAM L9

=> s 19

SAMPLE SEARCH INITIATED 17:03:32 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED 1 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 1 TO 80

PROJECTED ANSWERS: 0 TO 0

L11 0 SEA SSS SAM L9

=> s 19 full

THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS

DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y

FULL SEARCH INITIATED 17:03:38 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 78 TO ITERATE

100.0% PROCESSED 78 ITERATIONS

33 ANSWERS

SEARCH TIME: 00.00.01

L12 33 SEA SSS FUL L9

=> file hcaplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

157.94

358.03

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

0.00

-5.54

FILE 'HCAPLUS' ENTERED AT 17:03:41 ON 25 MAY 2004

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FILE COVERS 1907 - 25 May 2004 VOL 140 ISS 22  
 FILE LAST UPDATED: 24 May 2004 (20040524/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l12

L13 8 L12

=> s l13 and klar, u?/au

70 KLAR, U?/AU

L14 7 L13 AND KLAR, U?/AU

=> d his

(FILE 'HOME' ENTERED AT 16:55:55 ON 25 MAY 2004)

FILE 'REGISTRY' ENTERED AT 16:56:02 ON 25 MAY 2004

L1 STRUCTURE UPLOADED

L2 STRUCTURE UPLOADED

L3 1 S L2

L4 57 S L2 FULL

FILE 'HCAPLUS' ENTERED AT 16:58:27 ON 25 MAY 2004

L5 8 S L4

L6 7 S L5 AND KLAR, U?/AU

FILE 'CAOLD' ENTERED AT 16:59:09 ON 25 MAY 2004

L7 0 S L4

FILE 'HCAPLUS' ENTERED AT 16:59:19 ON 25 MAY 2004

L8 1 S L5 NOT L6

FILE 'REGISTRY' ENTERED AT 16:59:35 ON 25 MAY 2004

L9 STRUCTURE UPLOADED

L10 0 S L9

L11 0 S L9

L12 33 S L9 FULL

FILE 'HCAPLUS' ENTERED AT 17:03:41 ON 25 MAY 2004

L13 8 S L12

L14 7 S L13 AND KLAR, U?/AU

=> s l14 not 16



L15

0 L14 NOT L6

=>